mapping. Strains were computed from the gradients of the mapping. The accuracy of strain calculations was determined by simulating deformations of undeformed tag lines with a finite element (FE) model constructed from the undeformed image and comparing strains calculated with our method and the FE strains. The root mean square (RMS) error between FE strains and surface polynomial strains varied between 8.3 and 17.7% of the average FE strain for regions with six to nine tag intersection points. We have described a new method for calculating a transmural distribution of finite strains across the ventricular wall from MRI tissue-tagging and have quantified the accuracy of this technique. This algorithm may be applied to estimate the transmural distribution of regional strain in both ventricles non-invasively.

929-67 Reversibility of Ischemic Myocardial Injury can be Predicted by Gadolinium-DTPA Enhanced Magnetic Resonance Imaging After Reperfusion

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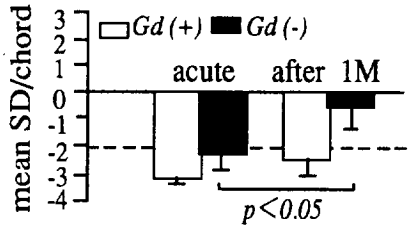
Reversible injured myocardium (stunned myocardium) due to brief ischemia demonstrates no enhancement in Gadolinium-DTPA enhanced magnetic resonance image (Gd-MRI) in animal studies. To test whether this finding can be observed in clinical settings or not, we studied 18 patients with acute myocardial ischemia using Gd-MRI. All patients underwent cardiac catheterization and angiography both on admission and after 1 month. In these patients, LAD was considered to be a culprit vessel and antero-septal region showed severe dyskinesis. If the flow grade was less than TIMI grade 3, PTCA was performed. With Gd-MRI (performed within 7 days), the patients were divided into two groups: Gd(+) and Gd(−). Gd(+) was defined as the group with the signal intensity ratio (anterior/inferior) higher than 1.20 in the ischemic area (normal control = 1.00 ± 0.08). LV wall motion was analyzed by using centerline method. Results are shown as follows:

	n	PTCA	mean SD/chord	
			acute	1 M
Gd(+)	11	11	3.17 ± 0.24	2.67 ± 0.71
Gd(−)	7	6	2.39 ± 0.59	0.65 ± 0.74



LV wall motion in Gd(+) couldn't improve at 1 month, but significantly improved in Gd(−). *Conclusion;* Dyskinetic myocardium without Gd-DTPA enhancement is regarded as reversible injured myocardium.

929-121 Impact of Ventricular Wall Curvature on Regional Function in Hypertrophic Cardiomyopathy: Assessment with MRI Tagging

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Because ventricular wall tension is related to wall curvature by the Laplace law, the curvature should affect regional wall function. We hypothesized that the ineffective (isometric) contraction of the interventricular septum observed in hypertrophic cardiomyopathy (HCM) may be related to its abnormal curvature. *Methods;* To address this issue, we studied 17 HCM patients with various septal morphologies and normal overall systolic function (mean echocardiographic fractional shortening, 48 ± 9%) using MRI tagging (spatial modulation of magnetization); there was asymmetric septal hypertrophy, prominent basal septal bulge and concentric hypertrophy in 7, 4, and 6 patients, respectively. Localized endocardial (endo %S) and epicardial (epi %S) intramyocardial circumferential shortening was measured in the septal and lateral walls on a basal short-axis slice. Short-axis curvature (SXC) and long-axis curvature (LXC) of the basal septal and basal lateral walls were determined as the reciprocal of the radius of the arc best fit to the wall curvature, which can be negative if the wall is convex to the LV cavity. Wall thickness was also measured at end-diastole. *Results;* Endo %S and epi %S were significantly lower in the septum than in the lateral wall, suggesting isometric septal contraction (20 ± 14 vs 45 ± 11%, $p < 0.0001$ for endo %S and 10 ± 9 vs 20 ± 11%, $p < 0.001$ for epi %S). Septal walls were flatter in the short-axis plane and more convex toward the LV cavity in the long-axis plane than lateral walls as indicated by smaller SXC and LXC (0.08 ± 0.03 vs 0.11 ± 0.03 mm^{-1} for SXC, −0.02 ± 0.02 vs 0.03 ± 0.01 mm^{-1} for LXC both $p < 0.0001$). There were significant correlations between %S and curvature and thickness as follows.

	septal wall		lateral wall	
	endo %S	epi %S	endo %S	epi %S
SXC	NS	NS	NS	r = 0.57
LXC	r = 0.56	r = 0.62	r = 0.55	NS
thickness	r = −0.63	r = −0.49	NS	NS

Multiple stepwise linear regression analysis showed that both wall thickness and LXC significantly contributed to %S in the septum (r = 0.79 for endo %S, r = 0.74 for epi %S, both $p < 0.005$). *Conclusions;* 1) Wall thickness and long-axis curvature appear to predict the septal function, whereas they have little impact on lateral wall function. 2) The thicker and more convex (toward the ventricular cavity) the septum is, the less it thickens in systole. 3) Isometric contraction of the interventricular septum in HCM may be partly due to its abnormal curvature.

929-122 Detection of Hybernating Myocardium by Dobutamine Magnetic Resonance Imaging

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Identification of hybernating myocardium (HM) by magnetic resonance imaging (MRI), is controversial. Trying to optimize MRI results we studied 45 pts with coronary artery disease (CAD) and depressed left ventricular wall motion (LVWM) and ejection fraction (LVEF) at baseline angiogram (ANGIO). MRI before and after a low doses infusion of dobutamine (DO, 5 mcg/kg/min). MRI defined LVWM and LVEF correlated with those of ANGIO (r = 0.767 and r = 0.843, respectively). After DO injection T1 signal increased in 27 (65 ± 15 vs. 98 ± 9, $p = 0.03$) pts whereas 18 pts had non significant changes (58 ± 12 vs. 52 ± 12, p = NS). All pts underwent coronary bypass surgery and repeated MRI before hospital discharge. LVEF (0.32 vs 0.45, $p = 0.03$) and LVWM (−2.6 ± 0.8 vs 0.8 ± 0.4 $p = 0.04$) improved in the 27 pts with T1 changes. None of the others improved LVEF (0.34 vs 0.36, p = NS) or LVWM (−2.4 ± 1.2 vs. −1.8 ± 0.7, p = NS). *Conclusion;* DO-MRI seems to be an effective manner to identify HM in pts with chronic CAD and depressed LV contractility.

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Monday, March 20, 1995, 3:00 p.m.–5:00 p.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 4:00 p.m.–5:00 p.m.

930-101 Cocaine Induced "Blood Doping" Maintains Myocardial Oxygen Delivery Despite Flow Limiting Coronary Vasoconstriction

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The mechanism whereby cocaine (COC) causes myocardial ischemia remains controversial. Most prior studies have suggested that COC induced increases in coronary resistance (CVR) coupled with increased myocardial O_2 demand (MVO_2) provided the substrate for ischemia. To determine whether COC induced CVR limits myocardial O_2 delivery, we studied 13 conscious dogs, chronically instrumented with LV pressure transducers, aortic and coronary sinus catheters, Doppler flow probe on the left circumflex coronary artery and atrial pacers. Coronary and MVO_2 responses were measured for 90 min following COC (1 mg/kg IV) in the intact state. Following COC, coronary blood flow increased rapidly (+30 ± 3% from 48 ± 2 ml/min, $p < 0.01$) within 2 mins but returned to baseline by 15 mins as CVR increased (+19 ± 4% from 2.1 ± 0.1 mmHg/ml/min) and remained elevated for 30 minutes. Despite flow limiting increases in CVR, myocardial O_2 delivery (+25 ± 6% from 7.1 ± 0.3 ml O_2/min) kept pace with the MVO_2 response (+27 ± 6% from 5.4 ± 0.3 ml O_2/min) to COC without requiring additional O_2 extraction after the first 2.5 mins. This was due to increased arterial O_2 content (+22 ± 4% from 15 ± 0.1 vol%, $p < 0.01$), which, in turn, was due to a significant increase in circulatory hemoglobin concentration (12.1 ± 0.4 g/dl to 14.2 ± 0.6 g/dl, $p < 0.01$) which persisted for 90 mins, well after hemodynamics had returned to baseline. Arterial oxygen saturation (97 ± 1%) and pH (7.41 ± 0.01) remained unchanged. Thus, COC induces a significant "blood doping" effect which contributes to the maintenance of myocardial O_2 delivery despite limi-

tations in coronary blood flow. The "blood doping" effect may provide a physiological explanation for the use of COC by athletes.

930-102 Coronary Denervation Attenuates Vasospasm Induced by Pericoronary Application of Methacholine in Pigs

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Autonomic innervation of the coronary arteries is thought to intervene in the genesis of coronary vasospasm. We assessed the potential effect of selective coronary denervation in the inhibition of vasospasm. Chronic sympathetic and parasympathetic denervation was provoked by topical application of phenol to the proximal LAD in 20 pigs through a lateral thoracotomy. Two weeks later, we performed an midsternal thoracotomy. Heart rate, aortic and ventricular (LV) pressure, LV dP/dt, coronary blood flow (CBF) at the LAD, and 32-channel epicardial ST segment mapping were monitored during every MCH application. Phenol-induced coronary adrenergic and cholinergic denervation was confirmed by histofluorescence and cholinesterase staining. Isolated LAD rings of 5 phenol-denervated pigs were studied to confirm smooth muscle integrity. Application of MCH to control pigs (n = 10) induced an statistically significant fall in CBF (75 ± 19%) accompanied by electrical and mechanical signs of ischemia: mean ST segment elevation on the epicardial electrograms of 9.7 ± 4.7 mV, a drop in systolic LV pressure (−20 ± 8.4 mmHg) and a decrease in LV dP/dt (−404 ± 203 mmHg/s). There were no changes in heart rate. The parameters returned to normal values after 5 to 8 min. As compared to controls, phenol treated pigs showed a significant attenuation of the fall in CBF (25 ± 17%), lesser ST segment elevation (2.4 ± 2.1 mV), a lower drop in LV pressure (−8 ± 2.3 mmHg), and a smaller decrease in LV dP/dt (−167 ± 104 mmHg/s). Coronary angiography performed in 6 additional pigs evidenced that the coronary spasm occurred at the site of MCH exposure. Isolated LAD rings of phenol treated pigs constrict after incubation with endothelin-1 indicating preserved vascular smooth muscle function. In 5 control pigs, a second application of MCH after muscarinic receptor blockade with atropine (0.4 mg/kg i.v.) resulted in complete abolition of the vasospasm confirming that vasospasm was mediated by the muscarinic receptor stimulation. In conclusion, pericoronary autonomic denervation protects against coronary constriction induced by direct muscarinic receptor stimulation with methacholine in situ the pig heart.

930-103 Endogenous Nitric Oxide Production Contributes to Increases in Coronary Blood Flow During Exercise

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Inhibition of nitric oxide (NO) production does not impair the normal ability to increase coronary blood flow (CBF) during exercise (Ex). We previously observed that K^+_{ATP} channel blockade decreased CBF at rest and during exercise, but K^+_{ATP} channel blockade either alone or in combination with adenosine blockade did not prevent exercise-induced increases of CBF. This study was performed to determine whether exercise-induced increases in CBF after K^+_{ATP} channel blockade and adenosine receptor blockade are dependent upon endothelial NO production. Ten dogs with a Doppler flow probe and microcatheter in the left anterior descending coronary artery were studied at rest and during 2 levels of treadmill Ex. Studies were performed during control conditions (CON) and then with the combination of glibenclamide (G) (50 μg/kg/min intracoronary) to produce K^+_{ATP} channel blockade and 8-phenyltheophylline (PT) (5 mg/kg iv) as an adenosine receptor blocker. Finally, measurements were repeated when NO production was inhibited by adding N-nitro-L-arginine (L) (1.5 mg/kg intracoronary). Data are mean ± SE.

	Heart Rate (beats/min)			CBF (ml/min)			CVC (×10^{-2}ml/min/mmHg)		
	Con	G+PT	G+PT+L	Con	G+PT	G+PT+L	Con	G+PT	G+PT+L
Rest	119±5	139±6$^{\#}$	134±10$^{\#}$	51± 4	29±3$^{\#}$	21±3$^{\#\dagger}$	59±5	32±4$^{\#}$	27±2$^{\#\dagger}$
Ex 1	191±5*	195±5*	188± 5*	77± 8*	37±5$^{\#}$	24±4$^{\#\dagger}$	91±10*	43±6$^{\#}$	29±6$^{\#\dagger}$
Ex 2	225±7*	219±7*	211± 8*	91±10*	49±6*$^{\#}$	32±5$^{\#\dagger}$	113±12*	58±7*$^{\#}$	34±5$^{\#\dagger}$

*$p < 0.05$ vs Rest, $^{\#}p < 0.05$ vs Con, $^{\dagger}p < 0.05$ vs G+PT; CVC = coronary vascular conductance

K^+_{ATP} channel blockade combined with adenosine receptor blockade decreased coronary blood flow, but did not block the increase in coronary blood flow in response to exercise. However, the subsequent addition of LNNA did block exercise-induced coronary vasodilation. Thus, when other vasodilator mechanisms are inhibited, endothelial production of NO can be shown to contribute to vasodilation of coronary resistance vessels during exercise.

930-104 Nitrate Tolerance: Impaired Vascular Effects of Stimulation and Inhibition of Nitric Oxide Release in Vivo

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Nitroglycerin (NTG) is metabolized to nitric oxide (NO) in vascular smooth muscle cells. It has been suggested that prolonged exposure to NO results in reduced vascular sensitivity to NO and/or down regulation of NO synthesis. Whether such changes contribute to the *in vivo* development of nitrate tolerance is currently not clear. This study investigates NO-mediated vasodilation in conscious rats before and after development of nitrate tolerance. Tolerance was induced by a 72 hours i.v. infusion of NTG and confirmed by a 68% reduction in the response to NTG (from 25 ± 3 to 8 ± 1 mmHg, $p < 0.05$, n = 7). The hypotensive effects of acetylcholine (ACh, endothelium dependent NO release, 10 μg/kg), and sodium nitroprusside (SNP, releases NO spontaneously, 20 μg/kg), were examined before and after infusion of NTG. Nitrate tolerance was associated with a attenuated hypotensive response to ACh (before 24 ± 3; after 17 ± 2 mmHg, n = 7, $p < 0.05$). Similarly, the response to SNP was reduced from 32 ± 1 to 26 ± 3 mmHg, n = 7, $p < 0.05$). Infusion of placebo (NTG solvens, n = 6) for 72 hours did not affect the response to ACh and SNP ($p > 0.05$). An effect of NTG treatment on endogenous NO regulation was further substantiated by the finding of a 62% reduction in the hypertensive response to the NO synthase inhibitor, L-NAME (n = 6), after induction of nitrate tolerance (from 29 ± 6 to 11 ± 1 mmHg, $p < 0.05$). The results suggest that prolonged infusion of NTG attenuates the vasodilator effects of NO, whether it is derived from the endothelium (ACh) or from exogenous sources (SNP) and that reduced vascular sensitivity to NO-dependent vasodilation may contribute to the development of nitrate tolerance in vivo.

930-105 Xanthine-Oxidase Inhibition Improves Coronary Endothelium-Mediated Relaxation in Patients with Early Atherosclerosis

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Atherosclerosis impairs endothelium-mediated relaxation (EMR) in the human coronary artery. Endothelial xanthine oxidase (XO) generates superoxide anion, an inactivator of nitric oxide. In the hypercholesterolemic rabbit aorta, endothelial XO-induced superoxide anion production is reduced by oxypurinol, restoring normal EMR. We hypothesized that XO inhibition with allopurinol would improve coronary EMR in patients with atherosclerosis. To assess the effects of XO inhibition on EMR, we studied 18 patients (risk factors + mild atherosclerosis) with serial intracoronary infusions of acetylcholine (ACH) (10^{-8} to 10^{-6}M) before and after IV allopurinol (150 mg/m^2 over one hour) (n = 8) or placebo (n = 10). All patients received intracoronary infusions of an endothelium-independent dilator (adenosine [2.2 mg/min] or nitroglycerin [40 μg]). A blinded analysis of arterial responses was performed using automated quantitative angiography. In Placebo patients, serial responses to ACH were identical (−19 ± 4%/−18 ± 5%, p = ns) (expressed as percent change pre/post placebo). However, in Allopurinol patients, ACH responses were dramatically improved after IV allopurinol (−20 ± 5%/−10 ± 5%, p = 0.01). Allopurinol did not affect resting coronary dimensions. Endothelium-independent responses were similar in both groups. Thus, XO inhibition improves coronary artery EMR in patients with coronary risk factors and early atherosclerosis. This suggests that XO-generated superoxide anion, via destruction of nitric oxide, contributes to the impairment of EMR in coronary atherosclerosis.

930-106 Potentiation of Atrial Natriuretic Peptide Mediated Coronary Vasodilatation by Beta Adrenergic Stimulation

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Increases in circulating atrial natriuretic peptide (ANP) and norepinephrine (NE) occur during the evolution of heart failure. While NE may augment ANP synthesis, a modulating action upon the biological actions of ANP is unclear. In vitro, the beta-adrenergic agonist (βA) isoproterenol (ISO) down-regulates the ANP clearance receptor which indirectly augments the biologically active ANP receptor. In vivo, the βA antagonist propranolol attenuates natriuretic peptide mediated coronary vasodilatation. We therefore hypothesized that, in vivo, ISO would potentiate subthreshold coronary vasodilating actions of ANP. Five anesthetized dogs were instrumented to measure left circumflex (LCx) coronary blood flow (CBF). Intracoronary (IC) ANP (100 ng/bolus) was administered in the LCx before and after the IC-ISO (1 mg over 15 min). Acetylcholine (ACh 1 ng/kg) and sodium nitroprusside (SNP 100 ng/kg) were admin-